

**REMARKS/ARGUMENTS**

These Remarks are responsive to the Office Action mailed October 1, 2004 ("Office Action"). Claims 1, 5-6, 9-14, 16-18, 29-31, 35-36, 39, and 42 are pending in the application. Claims 1, 5-6, 13, 14, 16-18, 29 and 31 are amended. Support for the amendments may be found at page 6, lines 15-20 and page 7, lines 15-26 as well as throughout the specification, tables, and drawing figures. New claim 43 is directed to the subject matter previously recited in claim 1.

The Office Action rejects claims 1, 5-6, 9-14, 16-18, 29-31, 35-36, 39, and 42 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1, 5-6, 9-14, 16-18, 29-31, 35-36, 39 and 42 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

Claims 1, 5-6, 9-10, 13-14, 16-18, 29-31, and 35 are rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 4,721,673 ("Uren").

Claims 1, 5-6, 9-14, 16-18, 29-31, 35-36, and 42 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ward et al., "Improved Production of Chymosin in *Aspergillus* by Expression as a Glucoamylase-Chymosin Fusion," Bio/Technology, Vol. 8, 1995 ("Ward") in view of Uren, Li et al., "Functional implications of the 21-24 loop in recombinant prochymosin," Biochimica et Biophysica Acta 1384 (1998) 121-129 ("Li"), and Pedersen et al., "Investigations on the Activation of Bovine Prochymosin," Eur. J. Biochem. 94, 573-580, 1997 ("Pedersen").

Claim 39 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Ward in view of Uren, Li, Pedersen, further in view of US 2002/0164696 A1 ("Kappeler").

Applicant respectfully requests reconsideration of the rejections of the pending claims for the following reasons.

**Disqualification of Commonly Owned Publication Under 35 U.S.C. § 103(c)**

Applicant disagrees that Kappeler, alone or in combination with other references, renders obvious claim 39. First, the references relied on, including Kappeler, fail to establish a *prima facie* case of obviousness of claim 39 (including all the limitations of claims 29 and 1, from which claim 39 depends) for the reasons given below with respect to claims 1, 5-6, 9-14, 16-18, 29-31, 35-36, and 42. Additionally, this application (09/779,560) and Kappeler were, at the time the invention of this application (09/779,560) was made, owned by Chr. Hansen A/S. Kappeler is, at best, prior art under 35 U.S.C. § 102(e)/103. The provisions of 35 U.S.C. § 103(c) remove Kappeler as a reference in this application. Accordingly, the sole rejection of claim 39 should be withdrawn and claim 39 should be allowed.

**Specification, Informalities, and Claim Objections**

The Office Action requires capitalization of and insertion of generic terminology for trademarks that are used in the specification. Applicant believes that the specification properly sets forth the terms noted in the Office Action. Applicant notes with appreciation the withdrawal of the objections to claims 12 and 15 set forth in the previous office action.

**Claim Rejections – 35 U.S.C. § 112, Second Paragraph**

The Office Action rejects claims 1, 5-6, 9-14, 16-18, 29-31, 35-36, 39, and 42 as being indefinite under 35 U.S.C. § 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Office Action

requests Applicant to clarify the meaning of the term "about." While Applicant continues to maintain that the term "about" does not render claims indefinite, Applicant deleted it in the interest of expediting prosecution. Accordingly, the rejection of all of the pending claims as being indefinite, under 35 U.S.C. § 112, second paragraph should be withdrawn.

#### **Claim Rejections – 35 U.S.C. § 112, First Paragraph**

The Office Action rejects claims 1, 5-6, 9-14, 16-18, 29-31, 35-36, 39, and 42 under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement. Support for the presently claimed subject matter, particularly for the claimed range limitations, may be found on page 7, lines 15-17, of the specification. Additional support may be found in entire specification including the tables and drawing figures of this application. Accordingly, the rejection of all of the pending claims under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement should be withdrawn.

#### **Claimed Invention**

The claimed invention is directed to a method of providing a milk clotting composition that comprises at least two steps (i) and (ii). In step (i), a medium is provided that has a pH of 2.0 or higher that comprises chymosin activity and glucoamylase activity. In step (ii), the medium is subjected to a pH in the range of 1.0 to 1.99 for a period of time sufficient to inactivate at least 50% of the glucoamylase activity while maintaining at least 75% of the chymosin activity.

### Claim Rejections – 35 U.S.C. § 102

The Office Action rejects claims 1, 5-6, 9-10, 13-14, 16-18, 29-31, and 35, under 35 U.S.C. § 102, as being anticipated by Uren.

“A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” Manual of Patent Examining Procedure § 2131 (8th ed., rev. 2, May 2004) (quoting Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)).

Uren teaches a recovery and activation process for microbially produced bovine (such as a calf) prochymosin. Uren teaches *E. coli* transformed with a plasmid producing a DNA sequence that encodes a portion of the beta subunit of tryptophan synthetase fused to prochymosin. Uren, col. 6, ll. 5-20. Uren teaches numerous steps for producing chymosin and in one of those steps a solution of prochymosin is titrated to a pH of 2. Uren, col. 6, ll. 30-35. Uren does not teach any steps utilizing a pH lower than 2, nor does Uren disclose or suggest a medium having glucoamylase activity.

The claimed invention requires, among other limitations, a step (i) “providing a medium having pH of 2.0 or higher” which includes “chymosin activity and glucoamylase activity,” and a step (ii) of “subjecting said medium to a pH in the range of 1.0 to 1.99.” In contrast to the claimed invention, Uren teaches a pH of no less than 2, which fails to meet all of the limitations of claim 1. The rationale of the Office Action focuses solely on step (i) of the claim (i.e., a pH of 2.0 or higher) and does not show how Uren teaches or suggests both steps (i) and (ii) of the Applicant’s claims. In fact, Uren fails to disclose Applicant’s step (ii). Uren does not teach

every element of claim 1 and therefore does not anticipate the present claims. Thus, the rejection of claims 1, 5-6, 9-10, 13-14, 16-18, 29-31, and 35, under 35 U.S.C. § 102, is misplaced and must be withdrawn.

In addition, the Office Action fails to discuss how the process in Uren includes glucoamylase activity or reduction thereof while maintaining the claimed (minimum 75%) of chymosin activity. Uren does not teach or suggest a medium having glucoamylase activity together with chymosin activity. Uren discloses a fragment of tryptophan synthetase fused to prochymosin. Uren, col. 6, 11. 5-20. It was asserted in the Office Action that the inactivation of at “...least 50% or 90% of the *E. coli* glucoamylase activity while maintaining at least 85% of the recombinant chymosin activity...is an inherent feature of practicing the method of Uren et al.” Office Action, pp. 5 and 10-11. It is well established that anticipation by inherency may only be established by a showing that prior art necessarily includes the limitation of the claim which is not explicitly disclosed by the prior art. Transclean Corp. v. Bridgewood Services, Inc. 62 USPQ2d 1865, 1871 (Fed. Cir. 2002). Inherency may not be established by probabilities or possibilities. The mere fact that the unstated limitation may be present in prior art is not sufficient. Crown Operations International v. Solutia Inc. 62 USPQ2d 1917, 1922-23 (Fed. Cir. 2002). The Office Action fails to show any basis for the assertion that glucoamylase activity would necessarily result from the process of Uren much less that such glucoamylase activity is “deactivated.” Thus, the Office Action fails to set forth a *prima facie* case of anticipation and the burden to establish unpatentability of Applicant’s claims over Uren remains on the Patent Office.

Accordingly, the rejection of claims 1, 5-6, 9-10, 13-14, 16-18, 29-31, and 35, under 35 U.S.C. § 102, must be withdrawn.

### **Claim Rejections – 35 U.S.C. § 103**

The Office Action rejects claims 1, 5-6, 9-14, 16-18, 29-31, 35-36, and 42 under 35 U.S.C. § 103(a) as being unpatentable over Ward, in view of Uren, Li, and Pedersen.

"To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." Manual of Patent Examining Procedure § 2143.03 (8th ed., rev. 2, May 2004) (citing In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)). "Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art." M.P.E.P. § 2143.01 (8th ed., rev. 2, May 2004); see also In re Lee, 277 F.3d 1338, 1342-44, 61 USPQ2d 1430, 1433-34 (Fed. Cir. 2002).

"Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness." M.P.E.P. § 2143.02 (8th ed., rev. 2, May 2004) (citing In re Rinehart, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976)). "The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure." M.P.E.P. § 2143 (8th ed., rev. 2, May 2004) (citing In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)). Finally, "[w]hen evidence of secondary considerations such as unexpected results is initially before the Office, for example in

the specification, that evidence should be considered in deciding whether there is a *prima facie* case of obviousness.” M.P.E.P. § 2144.08 (8th ed., rev. 2, May 2004).

Ward teaches improved production of chymosin in aspergillus by expression as a glucoamylase-chymosin fusion protein. Ward teaches a process whereby pH 2 is provided to make pseudochymosin from prochymosin. Thereafter, the pH is raised to 4.5 to produce mature chymosin. Page 435. Ward does not teach or suggest reducing the pH below 2 at any stage of its process, nor that such a reduction may inactivate glucoamylase, while maintaining most of the chymosin activity. As discussed above, Uren also lacks any teaching or suggestion to lower the pH below 2 and thus cannot serve as a basis for modifying Ward to do so. As noted by the Office Action, Li teaches exposure of prochymosin to a pH of 2.0 and Pedersen teaches activation of prochymosin at pH 2.1. See Office Action, page 8. As discussed above, the claimed invention requires, among other limitations, a step (ii) of “subjecting said medium to a pH in the range of 1.0 to 1.99” (the medium comprising chymosin activity and glucoamylase activity having been provided in step (i) at a pH of at least 2.0). For at least this reason, the references of record fail to establish a *prima facie* case of obviousness of the claimed invention.

In addition, the data included in the application shows that by reducing the pH below 2.0, the glucoamylase activity is reduced significantly while the chymosin activity remains at a level of greater than 85%. For example, in tables 2.1 and 2.2 at pH values of 1.6, 1.7, and 1.8, respectively, the residual milk clotting activity remained above 85%. At the same time, the glucoamylase (GAM) activity fell from a GAM activity of 100% at pH 5.6 to 0%, 0.8%, and 13.1% for pH values of 1.6, 1.7, and 1.8 respectively. Nothing in the prior art of record teaches

or suggests this differential effect on chymosin activity relative to glucoamylase activity. These results are significant in illustrating unexpected advantages achieved by Applicant's claimed invention and must be considered in evaluating the obviousness of the claimed invention.

In addition, claims 13, 14, 16, and 17 depend from claim 1 and recite claim range limitations that further distinguish the claimed invention over the cited prior art. For example, claim 13 requires a pH in the range of 1.5 to 1.99. None of the references of record teaches or suggests a pH within this range. Applicant submits that claims 13, 14, 16, and 17 are allowable for the reasons discussed above in relation to the independent claim, and for the additional reasons that none of the references of record teaches or suggests a pH within the ranges recited in those claims.

For at least the foregoing reasons, claims 1, 5-6, 9-14, 16-18, 29-31, 35-36, and 42 are not obvious, under 35 U.S.C. § 103, over the combination of Ward, Uren, Li, and Pedersen.

Claim 39 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Ward in view of Uren, Li, Pedersen, further in view of Kappeler. As discussed above, Kappeler is not a reference that can be utilized in a rejection under 35 U.S.C. § 103. Thus, the rejection of claim 39 should be withdrawn. Additionally, the rejection of claim 39 should be withdrawn for the reason given with respect to the rejection over Ward, in view of Uren, Li, and Pedersen discussed above. Accordingly, claim 39 is in condition for allowance.

Applicant believes that this response addresses all of the issues raised in the Office Action. Applicant believes that claims 1, 5-6, 9-14, 16-18, 29-31, 35-36, 39, and 42 are in condition for allowance and notice to that effect is hereby solicited. Should any issues remain to

be discussed in this application, the Examiner is invited to contact the undersigned by telephone to resolve those issues in an expeditious manner and place the application in condition for allowance.

In the event any variance exists between the amount authorized to be charge to the Deposit Account and the Patent Office charges, please charge or credit any difference to the undersigned's Deposit Account No. 50-0206.

Respectfully submitted,

HUNTON & WILLIAMS LLP

By:

  
Stanislaus Aksman  
Registration No. 28,562

Jeff B. Vockrodt  
Registration No. 54,833

Dated: January 3, 2005

Hunton & Williams LLP  
Intellectual Property Department  
1900 K Street, N.W.  
Suite 1200  
Washington, DC 20006-1109  
(202) 955-1500 (telephone)  
(202) 778-2201 (facsimile)

\_\_\_\_/\_\_\_\_